and which is obtained by expression in a genetically engineered microorganism, selected from a group consisting of *E. coli* and yeast, and purifying said hPTH.

30. An intact, recombinant hPTH which is essentially pure and which reacts with antibodies against hPTH in a manner identical to the native hormone.

IN THE SPECIFICATION:

Please delete the brief description of Figure 9 found on page 9, lines 1-13 and insert in place thereof --Figures 9A-9D show the purification of recombinant hPTH medium including: Figure 9A, a chromatogram of the HPLC purification; in Figure 9B a chromatogram of the HPLC purification of fractions 32 and 33 from panel 9A (the peak of the recombinant hPTH is indicated in black); Figure 9C, an HPLC of one microgram standards hPTH (1-84); and 9D, a co-chromatogram of the recombinant PTH from panel 9B and one microgram standard of hPTH.--

REMARKS

Entry of the foregoing and removal of the finality of the rejection of January 13, 1997, pursuant to and consistent with 37 C.F.R. § 1.129 and reexamination and reconsideration of the above-captioned application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, and in light of the remarks which follow, are respectfully requested.

Newly added claims 29 and 30 differ from the claims previously submitted in terms of scope and content. Newly added claim 29, for example, relates to an essentially pure, intact recombinant hPTH, expressed in yeast or *E. coli,* which exhibits a maximal response which is greater than that achieved through synthetic hPTH. In view of the shortcomings of the *Brewer et al.* reference as discussed herein and the Examiner's acknowledgment of the art recognized inferiority of the purity of naturally isolated proteins, this claim appears to be specifically related to allowable subject matter

The disclosure has been objected to because the brief description of Figure 9 as amended did not correlate to the Figure itself. Applicants have amended Figure 9's brief description accordingly. Should the Examiner request or require

additional drawing corrections to correspond the labeling of Figure 9 more closely to its description, Applicants will be happy to proffer same.

Applicants note the Examiner's comment regarding the double patenting rejection, and hereby reassert their intention to overcome this rejection by the submission of a Terminal Disclaimer once patentable subject matter has been identified.

The Patent Office has objected to claims 27 and 28 pursuant to 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. According to the Patent Office, claim 27 is indefinite because the metes and bounds of "fully active in an adenylate cyclase assay" are not clear. Applicants respectfully submit that the term would be clear and definite to those of ordinary skill in the art. The term means that the resulting recombinant protein is as active in this particular type of assay as would be predicted for a pure protein of this type. Furthermore, the adenylate cyclase assay is a known procedure. It is respectfully submitted that those of ordinary skill in the art would know how to evaluate the activity of hPTH in accordance with the present invention.

The sole remaining rejection contained in the most recent Final Rejection was under 35 U.S.C. § 102(b), alleging that the claims are anticipated by or in the alternative, under 35 U.S.C. § 103 obvious over *Brewer et al.*, U.S. Patent No. 3,886,132. In short, the Patent Office has taken the position that *Brewer et al.* teach isolating hPTH from naturally occurring sources. Since these naturally occurring sources would not suffer from the complications of wet chemical synthetic production, the resulting purity would allegedly be expected to be comparable to recombinantly produced hPTH. Applicants respectfully traverse.

First, Applicants note copending application Serial No. 08/461,436 which relates to various methods of producing hPTH recombinantly. In rejecting those claims, the Examiner noted that "[i]t is generally recognized in the art that recombinant production of biologically important proteins is desirable, as they can be obtained in greater quantity and more reliably than as isolated from their natural sources, especially in the case of human proteins." Official Action of January 10,

1997, at page 6. How can that statement be reconciled with the rejection in this case? With all due respect, the Patent Office cannot have it both ways. If human proteins isolated from their natural sources are expected to be of inferior purity, then the prior art rejection in this case is unsubstantiated on the record. If isolation techniques were known in the art to produce inferior results when compared to recombinant technology, then the claims of this application are *per se* patentable. On the other hand, if the Patent Office wishes to retract the statement made in the copending application, then the motivation and reasonable expectation of success, which the Patent Office alleges to exist therein, are not supported on the record. In that case, the copending method claims are allowable.

Moreover, and with all due respect, the assumption that isolation in accordance with *Brewer et al.* is likely to provide hPTH at the level of purity described and claimed in the above-captioned application is not justified. While the impurities may be different, they can still exist. hPTH is a relatively fragile molecule, as acknowledged in the background section of *Brewer et al.* As such, there is always the possibility of multiple fragments of hPTH being present. Some or all of these might coelute during the isolated hPTH depending on their size, charge and method of purification.

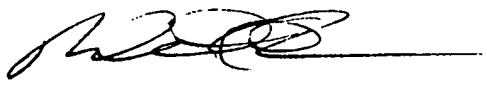
Second, there are numerous other biological molecules present in natural sources, in this case, the parathyroid gland. There is no reason based on *Brewer et al.* to assume that some or all of these proteins do not coelute with intact hPTH. In fact, in view of Dr. Maggio's prior uncontroverted testimony regarding the problems with the chromatographic techniques described in the prior art of record, there is far more reason to assume that isolated protein has a lower degree of purity, a factor implicitly recognized by the Examiner in this application's copending child. Finally, hPTH is present in very small amounts in its natural tissue. This also raises significant purity issues.

Under such circumstances, Applicants respectfully submit that it is incumbent upon the Patent Office to provide some form of substantiation of their position. On the record, it appears that Applicants have demonstrated significantly improved purity, purity which constitutes an unexpected result.

Should the Examiner have any questions with regard to the foregoing, or wish to discuss same, she should feel free to contact the undersigned, at the his convenience, at (908) 654-5000. Should any fee be due or owing in connection with this matter, the Examiner should charge Deposit Account No. 12-1095 therefor.

From the foregoing further and favorable action in the form of a Notice of Allowance is believed to be next in order and such action is earnestly solicited.

Respectfully submitted,
LERNER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK



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